UNITED STATES DISTRICT COURT
FOR THE DISTRICT OF NEW JERSEY

ASTRAZENECA PHARMACEUTICALS LP, *et al.* Plaintiff, v. TEVA PHARMACEUTICALS USA, *et al.* Defendant.	Civil Action No. 05-5333 (JAP) Consolidated Case: 06-1528 (JAP) Consolidated Case: 07-3001
ASTRAZENECA PHARMACEUTICALS LP, *et al.* Plaintiff, v. SANDOZ, INC., Defendant.	Consolidated Case: 07-1632 (JAP) **OPINION**

Plaintiffs, AstraZeneca Pharmaceuticals LP and AstraZeneca UK Limited (collectively "Astra" or "Plaintiffs"), have brought these consolidated actions against defendants Teva Pharmaceuticals USA, Inc., Teva Pharmaceutical Industries, Ltd. (collectively, "Teva"), and Sandoz, Inc. ("Sandoz," collectively with Teva, "Defendants") alleging infringement of U.S. Patent No. 4,879,288 (the "'288 patent") which covers the antipsychotic drug quetiapine. Presently before the Court are two motions by plaintiffs. First, Plaintiffs seek summary judgment

on the defense of inequitable conduct advanced by defendants.[1] Second, Plaintiffs seek to preclude certain of Defendants' claims of inequitable conduct as not being timely raised. For the reasons below, Astra's motion for summary judgment is granted, and Astra's motion to preclude is denied as moot.

I. Background

This case concerns the enforceability of the '288 patent, entitled "Novel Dibenzothiazepine Antipsychotic," which was issued in 1989 to a predecessor[2] of Astra for a compound known as quetiapine. AMF[3] ¶ 1. Since being approved by the FDA in 1997, quetiapine has been sold by Astra as an antipsychotic medication under the brand name SEROQUEL. AMF ¶ 47.

As noted in the '288 patent, early antipsychotic medications were "plagued by the problems of undesirable side effects." LDX 1 at col 1. These side effects include "acute dyskinesias, acute dystonias, motor restlessness, pseudo-Parkinsonism and tardive dyskinesias." *Id.* Antipsychotic drugs that pose the risk of causing these dyskinetic side effects are known as "typical" antipsychotics. *Id.*, AMF ¶ 54. Antipsychotics that are "non-dyskinetic," that is, they do not cause dyskinesias, are referred to as "atypical."

In the late 1960's and early 1970's a drug called clozapine was recognized as the first

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[1]The defense of inequitable conduct is the only issue remaining in this litigation, as all previously asserted defenses have been abandoned by Defendants.

[2]For simplicity, Astra's predecessor, ICI Americas Inc., is referred to herein as "Astra."

[3]The following abbreviations are used in reference to the record in this case: Astra's Rule 56.1 Statement ("AMF"); Teva's 56.1 Statement ("TMF"); Exhibits to the Declaration of Christopher Loh ("LDX"); Exhibits to the Declaration of John T. Bennett ("BDX"); Exhibits to the Declaration of Jason Harp ("HDX").

atypical antipsychotic drug. AMF ¶ 56. However, the use of clozapine was severely limited due to a serious side effect known as agranulocytosis, a fatal blood disease. AMF ¶ 57. Astra, therefore, in the late 1970's, undertook a project to develop another atypical antipsychotic. In 1985, chemist Edward Warawa and behavioral psychologist Bernard Migler discovered quetiapine, which showed reduced potential to cause dyskinesias, and Astra was ultimately issued the '288 patent in 1989.

A. '288 Patent Prosecution History

a. The Application

Astra's patent application, U.S. Patent Application No. 07/028,473 (the "'473 application") was submitted to the Patent and Trademark Office ("PTO") March 20, 1987. The application describes quetiapine, which it refers to as "Formula II," as an "invention concern[ing] a novel dibenzothiazepine compound useful for its antidopaminergic activity, for example, as an antipsychotic or neuroleptic." LDX 2. It goes on to describe "previous attempts at finding compounds useful in a variety of applications" that include U.S. Patent No. 3,539,573 to Schmutz, *et al.* ("Schmutz"), which "discloses selected dibenzothiazepines and debenzodiazepines as being useful for a variety of medical conditions including as neuroleptic-antidepressants, or neuroleptics" and U.S. Patent 4,097,597 to Horrom, *et al.* ("Horrom"), which discloses debenzodiazepine derivatives useful as antischizophrenics." *Id.*

After the references to these prior art compounds, the '473 application notes that "[c]ompounds used as antipsychotics and neuroleptics have . . . been plagued by the problems of undesired side effects." *Id.* These include "acute dyskinesias, acute dystonias, motor restlessness, pseudo-Parkinsonism and tardive dyskinesias." *Id.* As such, according to the '473

application, at that time "there still remain[ed] a need for compounds which exhibit antidopaminergic activity without the side effects heretofore experienced with previous compounds." *Id.* The '473 application states that quetiapine

> is useful because of its antidopaminergic activity, for example, as an antipsychotic agent or as a treatment for hyperactivity. Such a compound is of even greater interest in that it may be used as an antipsychotic agent with a substantial reduction in the potential to cause side effects such as acute dystonia, acute dyskinesia, pseudo-Parkinsonism as well as tardive dyskinesia which may result from the use of other antipsychotics or neuroleptics.

Id.

On November 2, 1987, Astra submitted additional information "believed to be pertinent to the examination of the ['473] application." LDX 3. Applicants provided a "list of references cited in the application and references believed to be relevant to the subject matter of the invention." *Id.* Listed are eight U.S. patent documents, two foreign patent documents and three other documents that include Research Disclosure 1980 ("Research Disclosure"), a German-language document, and an English-language abstract of Research Disclosure.

b. The First Rejection

By communication dated April 15, 1988, the examiner rejected all of the claims[4] in the '473 application for obviousness. LDX 4. First, the examiner found quetiapine unpatentable over the Schmutz II patent in view of Horrom or the references Fouche I or II, Umio or Research Disclosure 1980 ("Research Disclosure"). LDX 4 at 4. He noted that the closest prior art was column 10, lines 51-52 ("Schmutz X") and that "[t]his has unsubstituted ethylpiperazine whereas applicant has that ethyl substituted with hydroxyethoxy." The examiner further stated that "[t]he

[4]Claims 1-10 were pending in the application. Claims 9 and 10 were withdrawn and claims 1-8 were rejected. LDX 4.

secondary references teach this exact equivalence on compounds of very similar structure." "In short," according to the examiner, "applicants have simply made a modification known in 5 other tricyclic ring systems and done it on a 6th," and, further, that "one skilled in the art would realize this is a conventional modification, and when applied to the compounds of Schmutz II would obtain the claimed compound." LDX 4 at 5.

Second, the examiner rejected the claims as unpatentable over Horrom II in view of Schmutz II or the references Malen or Nakanishi. The examiner identified the closest prior art compound as Example 1 ("Horrom"), and noted Horrom differed from the claimed compound in that (1) it is a diazepine rather than a thiazepine, but identified references that taught "this precise equivalent;" and (2) Horrom has an 8-Halo while the claimed compound have 8-H, but noted that "the secondary references teach this." *Id.*

Third, the examiner rejected the claims as being unpatentable over Research Disclosure in view of the references Malen, Schneider or Nakashini. The examiner noted that Research Disclosure is an azepine rather than a thiazepine, and cited references that taught this equivalence. He also stated that Research Disclosure "is an 8-Halo rather than an 8-H of claims," and cited references that "teach this precisely." *Id.* at 6.

Last, the examiner rejected the claims as being unpatentable over Fouche II in light of the reference Malen. Referring to the "species of claim 8 of Fouche II, the examiner noted that the "sole difference is the central ring in the tricyclic ring system, in cycloheptadiene here and a thiazepine in the claim" and cited references teaching this equivalence. *Id.*

It appears that attached to this first rejection was the list of references Astra had submitted to the examiner in November 1987. *See* LDX 5. The initials "MB" appear next to each of the

references, indicating consideration of each reference by PTO examiner Mark Berch.

c. Response to the First Rejection

Astra submitted a response to the Examiner's initial rejection on October 19, 1988. In it Astra, among other things, addressed the examiner's obviousness rejections. Astra's attorney Thomas Jackson "preface[d] the discussion of the individual objections [with] some comments of general applicability to the determination of obviousness." LDX 5 at 4. He first explained that "typical antispychotics" were agents that treated psychosis without excessive sedation or life-threatening toxicity, but such agents had been associated with a range of troubling side effects. Examples of typical antipsychotics were identified as chlorpromazine, thioridazine, haloperidol.

The response then distinguished an "atypical" antipsychotic as a "clinically useful antipsychotic agent which exhibits a significant reduction in these side effects," and noted that quetiapine was an atypical antipsychotic. It identified clozapine as a clinically effective atypical antipsychotic, but noted that its use had been limited because of a sometimes fatal side effect. It then noted that "no atypical antipsychotic" is available for use in the United States." LDX 5 at 5. As such, Astra stated that "the problem sought to be solved in the instant case . . . is the discovery of an 'atypical antipsychotic.'" *Id.* Astra urged that

> the correct question of obviousness is whether references cited would teach one to seek to prepare the claimed compound as a solution to the problem of discovering an "atypical" antipsychotic agent. It is submitted that no such teaching is found in any combination of the cited references.

LDX 5 at 7 (emphasis in original). Astra then addressed the individual rejections by the examiner, arguing primarily that the non-dyskinetic properties of quetiapine were unexpected.

Astra also included and referred to within its response a "Formulae Sheet," which set forth the chemical structures of nine structurally-similar compounds to quetiapine: (1) clozapine, (2) loxapine, (3) clothiapine, (4) perlapine, (5) Schmutz X, (6) Schmutz Ex. 93, (7) Horrom, (8) a combination of the side chain of Horrom/21076 with the ring structure of Schmutz, (9) compound 21076.

c. The Second Rejection

Unpersuaded by Astra's arguments, on December 2, 1988, the examiner again rejected the claims. The examiner maintained two of his rejections from the April 15th action, again finding the claims to be unpatentable over Horrom (in view of Schmutz II and other references) and Schmutz II (in view of Horrom, Research Disclosure and other references). He found that a "prima facie case of obviousness has clearly been sent forth," in that "[o]nly very small differences separate the claims from the two prior art compounds" and the modifications were well known in the art. The examiner further stated that

> Once a condition of prima facie structural obviousness has been made out, it must be overcome by a side by side comparison with the closest prior art compound(s). In this case, one would test both the prior art species (example 1 of Horro[m] II and Column 10, lines 52-2 of Schmutz II) and the claimed specie for their ability to avoid, e.g., tardive dyskinesia (or whatever undesirable side-effect applicant wishes to focus on).

LDX 6 at p. 3 (emphasis in original).

Thus, the examiner advised that his obviousness rejection could be rebutted only by a comparison of quetiapine with the "closest prior art compounds(s)," which the examiner identified as Schmutz X and Horrom. With regard to other compounds, the examiner stated that "[t]he cited references are noted. None disclose compounds closer to the species than already

discussed." LDX 6 at 4.

d. Response to the Second Rejection

A response dated May 2, 1989, was submitted by Astra's attorney, James Jones, along with a declaration by Dr. Migler ("Migler Declaration"). In this response, Jones summarized the proceedings to date:

> [T]he Examiner took the position that the [quetiapine] is prima facie obvious over the combinations of references cited, and stated that the discovery of an additional property not disclosed in the references (i.e., that [quetiapine] is non-diskinetic [sic] as well as antipsychotic) does not make otherwise obvious compounds patentable. The Examiner has placed on applicants the burden of proving that the products disclosed in the prior art do not necessarily or inherently possess the characteristics of [quetiapine], as shown by a side-by-side comparison with the closest prior art compound(s). The Examiner has cited [Schmutz X and Horrom] as the closest prior art compounds for comparison with [quetiapine].

LDX 7 at 2.

Jones advises the examiner that the attached Migler declaration "is believed to be completely responsive to the showing required by the Examiner, although one point of difference does exist." *Id.* This difference was that, although the examiner identified Schmutz X as one of the two closest prior art compounds, "in place of this specific compound [Astra] offer[ed] data for the compound in Schmutz II" referred to as "Schmutz B". *Id.* Astra explained that it did not have data for Schmutz X, and that such data "would be very expensive to generate now." *Id.* With respect to the substituted compound, Astra stated that "[i]t is believed that [Schmutz B] actually more closely structurally resembles [quetiapine]" in that the hydroxyethyl substituent in Schmutz B's side chain more closely resembled quetiapine's hydroxyethoxyethyl substituent. *Id.*

Jones also noted that the Migler's declaration included data for a third compound, referred to as Schmutz A, which was not requested by the examiner. Astra explained that

> this compound has been chosen since it was cited in the list of Schmutz II compounds at columns 9-10 as having significant sedative and motility depressant action in standard test animals. The compound also bears some structural resemblance to [quetiapine] in that it has a substituted piperazinyl side chain.

Id.

After arguing Astra's position disputing the examiner's conclusion that a prima facie case of obviousness has been made out, Jones stated as follows:

> In any case, it is submitted that the [Migler declaration] submitted herewith is dispositive of the issue of whether compounds structurally resembling [quetiapine], and which might be expected to be antipsychotic, could also be expected to be non-diskinetic [sic] like [quetiapine]. By disposing of this issue, it is submitted that applicants have fully responded to the rejection maintained through the instant Office Action and have fully met the showing required by the examiner. It is noted that the data presented in the Declaration was generated as part of all the results generated in the normal course of research that led to the instant invention.

Id. at 3.

The Migler Declaration similarly described the purpose of Astra's submission. Dr. Migler states that

> under [his] direction and supervision experiments have been conducted that are probative of the issue of whether compounds structurally resembling [quetiapine] could also be expected to be non-diskinetic [sic] like [quetiapine]. Stated alternatively, the experiments show whether the prior art products hereinafter set forth necessarily or inherently possess the characteristics of [quetiapine].

LDX 8 at 2. Within the declaration, Dr. Migler sets out certain data comparing quetiapine, Schmutz A, Schmutz B and Horrom. He concludes by stating that "the data and results presented herein demonstrate that compounds which, by suitable tests, can be predicted to possess potential as antipsychotic agents, do not necessarily or inherently simultaneously possess the potential to be non-dyskinetic."

Shortly after the examiner received this second response and the Migler Declaration, the '473 application was allowed. LDX 9.

II. Discussion

A. Summary Judgment Standard

A court shall grant summary judgment under Rule 56(c) of the Federal Rules of Civil Procedure "if the pleadings, the discovery and disclosure materials on file, and any affidavits show that there is no genuine issue as to any material fact and that the movant is entitled to judgment as a matter of law." Fed. R. Civ. P. 56(c). The substantive law identifies which facts are critical or "material." *Anderson v. Liberty Lobby, Inc.*, 477 U.S. 242, 248 (1986). A material fact raises a "genuine" issue "if the evidence is such that a reasonable jury could return a verdict" for the non-moving party. *Healy v. N.Y. Life Ins. Co.*, 860 F.2d 1209, 1219 n.3 (3d Cir. 1988).

On a summary judgment motion, the moving party must show, first, that no genuine issue of material fact exists. *Celotex Corp. v. Catrett*, 477 U.S. 317, 323 (1986). If the moving party makes this showing, the burden shifts to the non-moving party to present evidence that a genuine fact issue compels a trial. *Id.* at 324. In so presenting, the non-moving party may not simply rest on its pleadings, but must offer admissible evidence that establishes a genuine issue of material fact, *id.*, not just "some metaphysical doubt as to the material facts." *Matsushita Elec. Indus. Co. v. Zenith Radio Corp.*, 475 U.S. 574, 586 (1986).

The Court must consider all facts and their logical inferences in the light most favorable to the non-moving party. *Pollock v. American Tel. & Tel. Long Lines*, 794 F.2d 860, 864 (3d Cir. 1986). The Court shall not "weigh the evidence and determine the truth of the matter," but need determine only whether a genuine issue necessitates a trial. *Anderson*, 477 U.S. at 249. If the

non-moving party fails to demonstrate proof beyond a "mere scintilla" of evidence that a genuine issue of material fact exists, then the Court must grant summary judgment. *Big Apple BMW v. BMW of North America*, 974 F.2d 1358, 1363 (3d Cir. 1992).

B. Inequitable Conduct

It is well established that patent applicants "have a duty to prosecute patent applications in the Patent Office with candor, good faith, and honesty." *Honeywell Int'l Inc. v. Universal Avionics Sys. Corp.*, 488 F.3d 982, 999 (Fed. Cir.2007). A breach of this duty constitutes inequitable conduct and renders the entire patent unenforceable. *Id.* Such a breach can arise from "an affirmative misrepresentation of a material fact, failure to disclose material information, or submission of false material information, coupled with an intent to deceive or mislead the [PTO]" *Purdue Pharma L.P. v. Endo Pharmaceuticals Inc.*, 438 F.3d 1123, 128 (Fed. Cir. 2006). Thus, to establish inequitable conduct, a challenger must show two things: (1) the patent applicant made an affirmative misrepresentation of a material fact, failed to disclose material information or submitted false material information; and (2) the patent applicant did so with an intent to deceive the PTO. *Cargill, Inc. v. Canbra Foods, Ltd.*, 476 F.3d 1359, 1363 (Fed. Cir. 2007). A party that claims that a patent is unenforceable due to inequitable conduct "must prove materiality and intent by clear and convincing evidence." *Id.* Thus, to survive summary judgment, Defendants in this case must introduce evidence from which a trier of fact could find materiality and intent by clear and convincing evidence. *Abbott Labs. v. TorPharm, Inc.*, 300 F.3d 1367, 1379 (Fed. Cir. 2002).

a. Materiality

For patent applications that were prosecuted prior to 1992, Federal Circuit has held that

"[i]nformation is deemed material if there is a substantial likelihood that a reasonable examiner would have considered the information important in deciding whether to allow the application to issue as a patent." *Ferring B.V. v. Barr Laboratories, Inc.*, 437 F.3d 1181, 1187 (Fed. Cir. 2006) (quoting 37 C.F.R. § 1.56 (1989)); *see also Li Second Family L.P. v. Toshiba Corp.*, 231 F.3d 1373, 1379 (Fed. Cir.2000); *Syntex (U.S.A.) LLC v. Apotex, Inc.*, 407 F.3d 1371, 1384 (Fed. Cir. 2005). The Court notes that this standard reflects an older PTO rule that was in effect at the time the patent-in-suit was prosecuted; the PTO amended the language of 37 C.F.R. § 1.56 in 1992. However, the Federal Circuit has expressly stated that it continues "to use the pre-1992 language regarding materiality for evaluating patents that were prosecuted before the amendment."[5] *Ferring B.V. v. Barr Laboratories, Inc.*, 437 F.3d at 1187 at n.6.

b. Intent

The second element that must be established is intent. "The intent element of inequitable conduct requires that the involved conduct, viewed in light of all the evidence, including evidence indicative of good faith, must indicate sufficient culpability to require a finding of intent to deceive." *Cargill,* 476 F.3d at 1365 (quotations omitted). Direct evidence of intent is not required, rather, "an intent to deceive is usually inferred from the facts and circumstances surrounding the conduct at issue." *Id.* Nevertheless, intent to deceive cannot be "inferred solely from the fact that information was not disclosed; there must be a factual basis for a finding of deceptive intent." *Hebert v. Lisle Corp.*, 99 F.3d 1109, 1116 (Fed. Cir.1996). Further, the Federal Circuit has noted that " 'materiality does not presume intent, which is a separate and

[5]Although the pre-1992 standard applies here, the Court notes that under the current materiality standard its decision with respect to the instant motion would be unchanged.

essential component of inequitable conduct.' " *Allen Eng'g Corp. v. Bartell Indus., Inc.*, 299 F.3d 1336, 1352 (Fed.Cir.2002) (quoting *Allen Organ Co. v. Kimball Int'l, Inc.*, 839 F.2d 1556, 1567 (Fed.Cir.1988)).

Defendants allege that several acts on the part of Astra constitute inequitable conduct and, therefore, render the '288 patent unenforceable. Defendants' first and primary argument is that Astra committed inequitable conduct because it misrepresented and/or omitted material information concerning certain prior art compounds in its prosecution of the '288 patent. Second, Defendants allege that, in response to a request by the patent examiner, Astra falsely asserted that generating data regarding a particular prior art compound would have been "very expensive." Third, Defendants claim Astra deceived the PTO by representing that a record reference taught that a particular compound was a typical antipsychotic. Last, Astra failed to disclose to the PTO the death of a cebus monkey during testing of quetiapine. The Court will discuss each of these below.

c. Balancing Test

If a party establishes the requirements of materiality and intent by clear and convincing evidence, a court must then engage in a balancing test. The court must "balance the equities to determine whether the patentee has committed inequitable conduct that warrants holding the patent unenforceable." *Cargill*, 476 F.3d at 1364. Under this balancing test, "[t]he more material the omission or the misrepresentation, the lower the level of intent required to establish inequitable conduct, and vice versa." *Id.* (quoting *Critikon, Inc. v. Becton Dickinson Vascular*

Access, Inc., 120 F.3d 1253, 1256 (Fed.Cir.1997)).[6]

C. Defendants Allegations of Inequitable Conduct

a. Internal Data on Prior Art Compounds

There appears to be no dispute that Astra's researchers synthesized and tested a great many compounds in the course of the research project to develop a potential dyskinesia-free antipsychotic drug and, consequently, had internal data on many compounds. Included among these were four prior art compounds: (1) perlapine; (2) fluperlapine; (3) compound 21076 (disclosed as Example f of the Research Disclosure publication); and (4) compound 24028 (disclosed as Example 40 of the Schmutz patent). According to Defendants, Astra had internal data showing that each of these four compounds were potential atypical antipsychotics, *i.e.*, they exhibited potential antipsychotic activity and had shown a reduced or eliminated potential to cause dyskinesias in tests. *See, e.g.*, HDX 6 at 41, 43. This internal data was never provided to the PTO, and Defendants allege that the withholding of this data by Astra constituted inequitable conduct.

The threshold determination in the inequitable conduct analysis is the materiality of the withheld data. Defendants contend[7] that data on these four compounds were "highly material" to the prosecution of the '288 patent for multiple reasons. First, they argue that the data contradicts "Astra's primary argument for the patentability of quetiapine" which Defendants allege was "that

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[6]In the instant case, in light of the Court's findings on the elements of materiality and intent as set forth herein, the Court does not reach this third step of the inequitable conduct analysis.

[7]The Court attributes the arguments raised to both defendants. Teva submitted an extended-length brief that Sandoz incorporated by reference into its own brief, which was more narrowly tailored and served to emphasize certain arguments raised in Teva's brief.

[quetiapine] possessed a combination of potential antipsychotic activity and reduced dyskinesias that purportedly was not possessed by prior art compounds that structurally resembled quetiapine." Teva Opp. Brf. at 16. *See also* Sandoz Opp. Brf. at 17 ("the pivotal issue was whether prior art compounds inherently possessed the property of being an atypical antipsychotic"). Second, Defendants argue that the data contradicted the Migler Declaration and that failing to disclose the data on these compounds rendered the declaration false and misleading. Last, they argue that even if the examiner was only interested in the "closest" prior art, Astra was obliged to turn over data on all structurally similar references and, therefore, this data was material.

As to Defendants' first argument, Astra asserts in response that Defendants' characterization of Astra's "primary argument for patentability" is built upon a misreading of the PTO prosecution and that, in fact, when the prosecution record is read objectively and in context it is seen that Astra did not make the argument attributed to it by Defendant. Rather, Astra argues that the record shows that the argument it made to the patent examiner was more specific, *i.e.*, that only the closest prior art compounds did not exhibit atypical antispychotic properties. This issue is significant because Defendants' materiality argument rests in large part on Defendants' claim that Astra's primary argument to the PTO was that *no* prior art compounds that structurally-resembled quetiapine possessed quetiapine's combination of properties (*i.e.*, antipsychotic and non-dyskinetic). Defendants, as the non-movants, expressly ask the Court to draw an inference from the record that "Astra repeatedly asserted to the PTO that quetiapine possessed a combination of potential antipsychotic activity and reduced dyskinesias that was not possessed by prior art compounds that structurally resembled quetiapine." Teva Opp. at 16. In

support, Defendants point to selected excerpts of the record that they argue support their characterization of Astra's argument. However, the Court may only draw inferences that are reasonable. The Court agrees with Astra that an objective, in-context reading of the record as a whole does not show that Astra made the argument claimed by Defendants.

Primarily, Defendants rely upon statements made in Astra's response to the second rejection which, according to Defendants, "invited" the examiner to "generalize from the reported results to other structurally similar compounds." TMF ¶ 90. For example, in that response, which accompanied the Migler Declaration, Astra's attorney Jones states that the "Declaration under Rule 132 submitted herewith is dispositive of the issue of whether compounds structurally resembling [quetiapine], and which may be antipsychotic, could also be expected to by non-diskinetic like [quetiapine]." LDX 8. However, the Migler Declaration (discussed in more detail below) states that the experiments described in the declaration address only the issue of whether the prior art compounds set forth in the declaration inherently possess the characteristics of quetiapine. The Court discerns no invitation to "generalize" the results to other compounds.

Defendants similarly point to portions the concluding paragraph of Jones's response which reads, in the relevant part as follows:

> It is accordingly submitted that the Declaration unequivocally shows that [quetiapine] not only possesses potential as an antipsychotic agent, but also, and very desirably, exhibits a significantly reduced probability for inducing undesirable dyskinesias. This combination of properties is nowhere suggested in any of the references of record. Further, as the Declaration abundantly demonstrates, this combination of properties is not automatically or inherently possessed by other compounds which may structurally resemble [quetiapine].

LDX 7.

The Court rejects Defendants' argument that the sentence that begins "This combination of properties . . ." was meant by Astra to mean that none of the prior art has the combination of qualities quetiapine possesses. Under a plain reading in the appropriate context, no reasonable factfinder could reach that conclusion. Astra is asserting that none of the references before the examiner suggest that quetiapine would have those qualities. Further, the reading ascribed to that sentence by Defendants would render the following sentence, which refers to "other compounds," redundant and nonsensical.

Defendants other references to the record in support of their position are equally unavailing. The Court finds that the record does not support Defendants' characterization of Astra's "primary argument" for patentability.

Similarly, the Court rejects Defendants' assertion that the data was material because the failure to disclose the data rendered the Migler Declaration misleading. Defendants allege that the declaration was submitted to the PTO as evidence that, as a general matter, no compounds that structurally resemble quetiapine share its combination of properties. Teva Opp. Brf. at 23. In support of this argument, Defendants refer to that part of the declaration that states "Under my direction and supervision, experiments have been conducted that are probative of the issue of whether compounds structurally resembling [quetiapine], which could be expected to be antipsychotic, could also be expected to be non-diskinetic like [quetiapine]." LDX 8 at 2. However, Defendants' argument completely ignores the very next sentence in the declaration, which states, "*Stated alternatively*, the experiments show whether the prior art products *hereinafter set forth* necessarily or inherently possess the characteristics of [quetiapine]. *Id.* (emphasis added). Given Dr. Migler's clarification in the second sentence, no reasonable

inference can be drawn that the earlier sentence was meant to assert a general argument that no other antipsychotic compounds that structurally resembled quetiapine could be expected to be non-dyskinetic. As such, nothing about the failure to disclose the data on the four compounds renders the declaration false or misleading.

Finally, Defendants argue that even if a reasonable examiner was only interested in the closest prior art, the data on the four compounds are nonetheless material. The law is clear that to overcome a prima facie structural obvious rejection, an applicant must provide evidence comparing the invention to the closest prior art. *See In re Merchant*, 575 F.2d 865, 869 (CCPA 1978). In asserting that Astra was nevertheless obligated to provide data on the four compounds at issue, Defendants rely primarily upon *In re Holladay*, 584 F.2d 384 (CCPA 1978), *In re Payne*, 606 F.2d 303 (CCPA 1979) and *In re Johnson*, 747 F.2d 1456 (Fed. Cir. 1984). Teva Opp. at 24-26. However, the Court finds these cases do not help Defendants. In *Holladay*, the court confirmed that "[a]n applicant relying upon a comparative showing to rebut a prima facie case must compare his claimed invention with the [c]losest prior art." 584 F.2d at 386 (quoting Merchant, 575 F.2d at 869). The court noted that "in most cases, the closest prior art will be the art relied on by the examiner," but that "[i]t is conceivable that two or more pieces of prior art could be equally close to the invention, and yet only one of them applied against the claims by the examiner." *Id.* In such cases, the court found that "there is no logical reason for requiring an applicant to make a comparison with one instead of the other." *Id.* Thus, *Holladay* establishes that where two pieces of prior art are shown to be equally close to the claimed invention, there is no reason to insist that the applicant compare his invention with the one relied upon by the examiner.

In *Payne*, a case involving claimed pesticide compounds, the court found the applicant had failed to rebut a prima facie case of obviousness. In that case, the applicant had submitted test data on only one of the several compounds cited by the examiner. In doing so, the court confirmed that an applicant need not test the compounds taught in every reference but "where an applicant tests less than all cited compounds, the test must be sufficient to permit a conclusion respecting the relative effectiveness of applicant's claimed compounds and the compounds of the closest prior art." 606 F.2d at 316. Here, Astra submitted data on one compound to the examiner and offered substituted data for the second compound identified by the examiner, and the examiner accepted the substitution.

The court in *Johnson* again reaffirmed that an applicant must compare the invention to the closest prior art. 747 F.2d 1456. *Johnson* involved a case in which the applicant claimed a novel chemical compound having herbicidal activity. The examiner rejected the claims as obvious over compounds disclosed in three prior art references. The applicant submitted a Rule 132 declaration comparing the applicant's compound with a representative compound from one of the cited references. The examiner maintained the rejection, noting that an additional compound disclosed in a second prior art reference was equally close to the claimed compounds, and thus a showing of unexpected results over this additional compound had to be submitted to overcome the rejection. The applicant did not submit data on the second compound specified by the examiner, but argued on appeal that, in light of *Holladay*, it was not necessary to make an additional comparison because an applicant is required to compare his invention only with one of equally close prior art references. The Federal Circuit affirmed the rejection, finding that the applicant did not provide sufficient evidence to rebut the Examiner's conclusion of obviousness

because he had neither established nor asserted that the teachings of both of the references were so parallel that a comparative test with one of the references would suffice to show relative effectiveness over the other prior art disclosure. Thus, *Johnson* addresses an applicant's duty of comparison when there are two equally close references. That is simply not an issue presented here, as the examiner expressly specified the comparison Astra would be required to make.

In sum, the Court finds that Defendants have not established the claimed "high" materiality of the withheld data. There is no dispute that Astra disclosed certain prior art references to the PTO examiner that described perlapine, fluperlapine, 21076 and 24028. Accordingly, the examiner considered the compounds as well as their chemical structures. After such consideration, the examiner rejected the quetiapine as structurally obvious two separate times. In his second and final rejection, he found quetiapine to be structurally obvious in view of Schmutz X and Horrom, and advised Astra that the prima facie case of obviousness could only be overcome by a "side-by-side comparison" of these compounds with quetiapine that showed that the Schmutz and Horrom compounds did not exhibit atypical antipsychotic properties. LDX 6 at 3. The examiner expressly laid out for Astra exactly what it needed to do: "In this case, one would test both prior art species (example 1 of Horro[m] II and Column 10, lines 52-2 of Schmutz II) and the claimed specie for their ability to avoid, e.g., tardive dyskinesia (or whatever undesirable side-effect applicant wishes to focus on)." The Migler Declaration and the response from Astra's attorney followed. It is undisputed that Astra did not have data on Schmutz X and, therefore, proffered a substitute, Schmutz B, to the examiner. The examiner accepted the substitution and allowed the claims. Under these undisputed facts, as detailed in the discussion above, the data on the four compounds simply was not "highly" material.

Even if Defendants had shown the data to have some degree of materiality, Defendants would still be required to present evidence showing Astra's intent to deceive. However, Defendants' showing is lacking in this regard. The Court recognizes that intent need not be proven by "smoking gun" evidence, but rather is often inferred from circumstances surrounding the conduct. *Cargill,* 476 F.3d at 1365 . Nevertheless, to defeat summary judgment, the Defendants must present some evidence from which the Court can draw inferences regarding intent. *Hebert v. Lisle Corp.*, 99 F.3d 1109, 1116 (Fed. Cir.1996) (intent cannot be "inferred solely from the fact that information was not disclosed; there must be a factual basis for a finding of deceptive intent."). With respect to intent, Defendants in large part rely upon their assertion of the "high" materiality of the withheld data. The also point to the alleged contradictions between the data and Astra's arguments to the PTO. However, the Court has rejected these assertions as unsupported in the record. Additionally, Defendants could not rely upon materiality alone, as "materiality does not presume intent, which is a separate and essential component of inequitable conduct." *Allen Eng'g Corp. v. Bartell Indus., Inc.*, 299 F.3d 1336, 1352 (Fed.Cir.2002).

Defendants also allege that intent to deceive can be inferred because Astra allegedly had multiple opportunities to disclose the data to the PTO but did not. They also assert that the fact that four compounds were involved show that the nondisclosure could hardly be "accidental." Teva Opp. at 38. Given the undisputed prosecution history, the Court finds these arguments to be completely without merit.

Much of Defendants other evidence of intent is little more than mere speculation. For example, Defendants allege Astra had a "strong motive" to deceive the PTO because it knew that "patenting quetiapine would be difficult" and the resources it had invested into developing the

drug would be "wasted" if the patent application failed. Aside from the lack evidentiary support that this was genuinely a concern for Astra, the alleged "motive" proffered by Defendants amounts to nothing more than a general business interest in obtaining a patent. It does not show that Astra intended to engage in deception to obtain it. *See In re Oxycontin Antitrust Litigation*, 530 F. Supp. 2d 554, 563 (S.D.N.Y. 2008) (vague allegations that applicant had strong business desire to obtain a patent for its drug, "if credited, . . . would show only that [the applicant], like any patent applicant, had a strong desire to see its invention patented, and not that it intended to engage in deception in order to accomplish that goal.")

Defendants also point to the assertion by Astra that generating Schmutz X data would be "expensive" as evidence that Astra intended to deceive the PTO. Defendants claim that such a representation was untrue (but as discussed below, the Court finds Defendants' evidentiary basis lacking for this allegation), and that Astra lied because it had reason to be concerned that if it tested Schmutz X the data would be unfavorable to their application. However, Defendants admit that the test results of Schmutz X could not be predicted. Multiple layers of sheer speculation cannot give rise to an inference of intent to deceive.

In sum, even if Defendants had shown that the withheld data on the four compounds was material, Defendants have not proffered sufficient evidence to raise the inference that Astra intended to deceive the PTO when it failed to provide its internal data on perlapine, fluperlapine, compound 24028 and compound 21076. Summary judgment is granted as to Astra on this issue.

b. Expense of Generating Data

As noted above, after twice rejecting the claims to quetiapine for obviousness, the PTO examiner "placed on applicants the burden of proving the products disclosed in the prior art do

not necessarily or inherently possess the characteristics of [quetiapine], as shown by a side-by-side comparison with the closest prior art compound(s)." LDX 7. The examiner specified that the closest prior art compounds were Horrom and Schmutz X. In response, Astra provided the examiner with data comparing quetiapine to three other prior art compounds: Horrom, Schmutz A and Schmutz B. Astra did not give the PTO examiner test results for Schmutz X, one of the compounds identified by the examiner as structurally closest to quetiapine. Rather, Astra advised the examiner that it did not have data regarding Schmutz X and, further, that "such data would be very expensive to generate now." LDX 7 at p. 2. It is undisputed that Astra did not have data on Schmutz X. However, Defendants allege that Astra's assertion that the Schmutz X data would be too expensive to produce was false and that the real reason was "more likely"[8] that Astra was uncertain about what the results of such testing would show. According to Defendants, Astra had test data showing a closely related compound to Schmutz X, the compound 24028, had proven to be potentially active with low dyskinesias like quetiapine. Thus, Defendants argue that Astra's representation that generating the data would be "expensive" was false and made with the intent to deceive the PTO examiner, and, therefore, it constitutes inequitable conduct on the part of Astra.

In support of their argument that Astra's representation was false, Defendants point to the testimony of Dr. Warawa, who stated that, "from the standpoint of chemistry," it would not be expensive to synthesize Schmutz X. BDX 16 at 200. Sandoz also submitted an opinion from an expert who agreed that synthesizing the compound would not be expensive. HDX 2. However, Dr. Warawa testified that he believed the reference to expense was "on the pharmacological side,

[8]Sandoz Opp. at 7.

the testing side," and Dr. Migler testified that generating the requested test data would "take time away from ongoing research work" and "[r]emoving technicians from their ongoing work would be expensive." LDX 31 at 292. While one of Sandoz's experts opines, with little detail, that "it would have been a relatively trivial undertaking to carry out these tests" because the colony of animals was still operational and continuing in use for similar tests of other compounds, the expert does not address, much less contradict, Dr. Migler's testimony that taking technicians away from ongoing work would have been expensive. Defendants, therefore, have failed to raise a material fact issue regarding the falsity of Astra's statement.

Moreover, Defendants have failed to establish that there exists a triable issue regarding the materiality element of the inequitable conduct analysis. The PTO examiner twice rejected the application on the basis of obviousness and indicated that prima facie obviousness "must be overcome by side-by-side comparisons with the closest art compound(s)." LDX 6. That being the requirement, the expense of performing such comparisons could hardly be considered "important" to a reasonable patent examiner in deciding whether to allow the patent to issue. Applying the relevant materiality criteria, the Court finds the representation regarding the cost of generating the requested data to be immaterial.

Given the Court's findings with respect to allegations of falsity and materiality, it is clear that there is no support for Defendants' claims with respect to the second element of the inequitable conduct analysis, *i.e.*, that Astra intended to deceive the PTO with respect to the cost of obtaining the requested Schmutz X data. Consequently, summary judgment of no inequitable conduct is granted to Plaintiffs with respect to this issue.

c. Statement Regarding Research Disclosure Reference

Among the bases stated in his first rejection of the '473 application, the PTO examiner noted that quetiapine was "unpatentable over Research Disclosure in view of Malen, Schneider or Nakashini." LDX 4 at 5. The examiner referred specifically to compound 21076. *Id.* In its response to this first rejection, Astra's attorney stated that "As noted above, Research Disclosure 1980 exemplifies and claims the compound of formula 9, among others, as a 'typical' antipsychotic; there is no teaching concerning an 'atypical' antipsychotic, the problem sought to be solved in the instant case." LDX 5 at 11.

Defendants allege that Astra mislead the PTO examiner by representing that Research Disclosure was a typical antipsychotic. According to Defendants, this prior art reference discloses a series of compounds described only as "neuroleptics" or "acting neuroleptically," and such descriptions, at the time Research Disclosure was published (1980), meant that a compound had potential antipsychotic but allegedly did not teach anything with respect to a compound's dyskinetic potential. Defendants note that although the examiner was provided with the Research Disclosure by Astra, it was provided to the examiner in its original German and had not been translated. However, Astra did provide the examiner with an English-language chemical abstract that summarized the Research Disclosure reference.

Defendants further argue that Astra had motive to mislead the examiner with respect to compound 21076. Defendants allege that 21076 was structurally as close or closer to quetiapine than other prior art compounds, and since Astra allegedly had data showing that 21076 was potentially an atypical antipsychotic, Astra had reason to "divert the Examiner's attention away from the Research Disclosure reference." Teva Brf. at 43.

Astra responds first by arguing that it did not misrepresent what the prior art Research Disclosure reference taught. Astra's attorney represented that the disclosure described typical antipsychotics. Astra asserts that Research Disclosure contained no reference to atypical properties, and, as such, the reference could not have been read as disclosing them. This being so, according to Astra, the disputed representation was not false.

Astra, citing *Innogenetics, N.V. v. Abbott Labs*., 512 F.3d 1363, 1379 (Fed. Cir. 2008) ("Given that the [prior art reference] had been submitted for the patent examiner to examine herself, she was free to accept or reject the patentee's arguments distinguishing its invention from the prior art.") and *Akzo N.V. v. U.S. Int'l Trade Comm'n*, 808 F.2d 1471 (Fed. Cir. 1986) ("The mere fact that Du Pont attempted to distinguish the Blades process from the prior art does not constitute a material omission or misrepresentation. The examiner was free to reach his own conclusion regarding the Blades process based on the art in front of him."), further argues that its characterization of the Research Disclosure reference was not material. It provided the Research Disclosure reference as well as an English-language abstract of it to the examiner. Thus, Astra asserts that the examiner could reach his own conclusion about what the reference taught.

Lastly, Astra points to the fact that it provided the Research Disclosure reference and the abstract as evidence of its good faith and lack of intent to deceive the PTO.

The Court finds that Defendants have not established that a genuine issue of material fact exists with respect to the relevant elements of inequitable conduct. First, the instant case is distinguishable from the case relied upon by Defendants, *Semiconductor Energy Laboratory Co., Ltd. v. Samsung Electronics Co., Ltd.*, 204 F.3d 1368 (Fed. Cir. 2000). In that case, the court held that an applicant effectively failed to disclose a material reference to the PTO where the

record reference was in Japanese and the applicant provided a "one-page, partial translation focusing on less material portions and a concise statement directed to these less material portions," thereby leaving the PTO examiner "with the impression that the examiner did not need to conduct any further translation or investigation." *Id.* at 1377.

Here, Defendants do not argue that the English-language abstract provided to the examiner was misleading or incomplete in any way. Rather, Defendants challenge the characterization by Astra's attorney of the Research Disclosure reference to the examiner. However, the examiner presumably had considered at least the English-language abstract of the disclosure, and, therefore, could draw his own conclusions. There could have been nothing in Astra's mere characterization of a reference already provided the to examiner that could have left the examiner "with the impression that the examiner did not need to conduct any further translation or investigation." To the contrary, if Astra's characterization was inconsistent with the examiner's understanding of the reference based on his review of the abstract, it would have served only to highlight to the examiner that more investigation or translation was necessary. The Court, consequently, finds that Astra's characterization was not material.

Further, the fact that Astra voluntarily disclosed the reference to the examiner and gave him the Research Disclosure reference as well as the English-language abstract severely undercuts an argument that there was an intent to deceive. Defendants have simply not met their burden to show there exists a triable issue of fact as to alleged inequitable conduct, and, therefore, summary judgment is granted in favor of Astra.

d. Toxicity of Quetiapine

The '473 application that states that the therapeutic dosage of quetiapine in humans was

"about 1.0 to 40 mg/kg per day," and further states that "[n]o overt toxicity has been observed for this compound at therapeutic doses." LDX 2 at 9. Defendants argue that Astra's representation regarding "overt toxicity" is false, because during animal testing of quetiapine a cebus monkey died after being given a dose of the compound within the specified range of therapeutic doses.

A declaration by Dr. Migler submitted to the PTO describes a test using cebus monkeys which is used to evaluate the dyskinetic properties of test compounds. LDX 8. In performing this test, a cebus monkey is given a dose of a test compound and the monkey is observed over the next several hours for dyskinetic reactions. In one such test, quetiapine was administered to five monkeys at a dose of 40 mg/kg, along with a number of other monkeys being given quetiapine in different dosages.[9] One of the monkeys given the 40 mg/kg dosage died shortly after administration of the drug. The death of this monkey was not disclosed in the quetiapine data provided to the PTO.

Defendants contend that the failure by Astra to disclose the monkey's death to the PTO amounts to inequitable conduct. Defendants note that in at least one subsequent cebus monkey test conducted by Astra, a dose of less than 40 mg/kg was selected for testing as a result of the earlier monkey death. BDX 10. Defendants argue that the data on the monkey's death was material because in contradicted the statement in the '473 application that "[n]o overt toxicity" had been shown at clinical doses. As such, the monkey's death would be material, if at all, only if it was caused by the toxic effects of quetiapine.

A necropsy was conducted on the monkey and the resulting report did not state a cause of

[9]A total of 57 monkeys were tested. LDX 8 at 5.

death. LDX 38. The report indicates the monkey's death occurred approximately 15 minutes after dosing, although a notation in lab notebook indicates that the monkey died 45 minutes after dosing. *See* LDX 37, 38. The report also indicated a finding of fluid in the monkey's lungs. Dr. Migler testified that he believed the monkey may have died as a result of the dose being improperly injected into the monkey's lungs. BDX 15 at 343. He also stated that death from such an injection would occur rapidly but, if the notation in the lab notebook regarding the time of death rather than the necropsy report was accurate, such an explanation would not be consistent with a 45 minute time frame. BDX 15 at 350. However, while there may be some dispute concerning the circumstances of the monkey's death, Defendants have pointed to nothing in the record that shows that the monkey died from the toxic effects of quetiapine; such a conclusion is speculative at best.

Nevertheless, even if the Court were to conclude that fact issues preclude a finding with respect to materiality, there is no evidence from which the Court can infer that this information was withheld with the intent to deceive the PTO. For example, Defendants speculate that Astra was motivated "not to call to attention any data that may make the Examiner question the safety of quetiapine" because Astra had noted in its first response to the PTO that the use of clozapine was limited because of certain severe side effects. Teva Opp. at 45. The Court finds this to be wholly insufficient to raise an inference of deceitful intent. Having failed to establish that there exists a genuine issue of material fact with respect to this issue, the Court grants summary judgment in favor of Astra.

III. Conclusion

In opposing this motion, Defendants have argued to the Court the necessity of a trial in

order for the parties to present expert testimony and to allow the Court to make credibility determinations with respect to fact witnesses. The Court finds this to be a facile argument. While the Court recognizes on summary judgment it cannot make findings of credibility, there are no credibility determinations to be made here; the prosecution record speaks for itself. Moreover, experts engaging in hindsight cannot change the facts and circumstances of the patent application process that occurred two decades ago. For the reasons above, Astra's motion for summary judgment is granted, and its motion to preclude is denied as moot. An appropriate Order accompanies this Opinion.

/s/ JOEL A. PISANO
United States District Judge

Dated: July 1, 2008